REMARKS

Reconsideration of this application is requested.

Non-elected claims 5-9 have been cancelled without prejudice to divisional filing.

An abstract has been provided as required in ¶ 7, page 3 of the action.

The Examiner's comments in ¶ 8 regarding benefit of an earlier application have been noted. It appears that the Examiner overlooked the applicants' amendment of July 26, 2000 wherein reference to applicants' PCT filing was inserted as the first sentence, page 1 of the application. See Box 11, page 2 of applicants' original transmittal letter. In any case, it is proposed to complete the earlier amendment to add reference to the EP priority application as well as the PCT filing. It is believed that the previous amendment and present amendment in this regard are appropriate but, if the applicants need to do anything more, the Examiner is requested to advise.

Claim 4 has been amended to obviate the dependency objection thereto.

Reconsideration of the Section 112, 2nd ¶ rejection of claims 1-4 is requested in view of the amendments to claim 1. These amendments should obviate the Examiner's objection to claim 1 as these objections are set out in the last two ¶s, page 4 of the action. Thus, claim 1 has been amended to indicate that each nucleic acid sequence is from the referenced repertoire, as suggested by the Examiner.

Additionally, claim 1 has been amended to indicate that the encoded at least part of the variable domain retains its ability to exhibit antigen binding activity. Basis for this amendment is found at, for example, page 9, last ¶ of the applicants' disclosure.

The Examiner is requested to reconsider the objection to the claim language "cloned from non-immunized source". It is believed that this language is clear and definite and fully understandable by those in the art. Thus, it will be known that a non-immunized source is a source which has not been immunized with predetermined antigens. Immunized sources are those organisms where an antigen has been injected into the source from the external environment. For non-immunized sources there has been no pre-immunization of the donor with the target antigen.

The Examiner is also requested to reconsider the Section 102(a) rejection of claims 1-4 as anticipated by Casterman et al, U.S. 5,800,988. The patent does not disclose an expression library comprising a repertoire of nucleic acid sequences cloned from a non-immunized source.

The reference in Column 14 of Casterman to the preparation of antibodies without a previous immunization is not made in the context of anything resembling the applicants' invention.

The same comments are true with respect to the rejection of claims 1-4 based on EP 584 421 which is discussed and distinguished in the applicants' specification. See, in particular, pages 4-6 of the applicants' disclosure, beginning with page 4, line 24. Accordingly, reconsideration and withdrawal of the Section 102(b) rejection based on the EP disclosure is requested.

More specifically, both Casterman et al and the EP reference relate to methods of isolation of VHH which are not related to the applicants' libraries. Both references disclose several methods by which VHH (heavy chain antibodies) can be isolated such as

(a) direct purification from blood;

(b) use of standard hybridoma cell techniques for generating monoclonal antibodies; and

(c) use of cDNA libraries.

The "non-immunized" remark in Column 14 of Casterman and the corresponding comment in EP 584 421 only refer to the method (b) which is use of hybridoma cell line techniques. The use of libraries is described in Column 14, lines 20-40 and explicitly refers to the use of a previously immunized source in line 26. There is, therefore, clearly no disclosure of the applicants' expression library in either Casterman or EP 584 421.

Reconsideration of the Section 102(b)/103(a) rejection of claims 1-4 based on Ghahroudi et al is requested. This reference does not disclose the applicants' library or make it obvious. Clearly, the Examiner cannot disregard the applicants' claim limitation "cloned from a non-immunized source" as, in essence, a non-substantive process feature. There are fundamental differences between nucleic acid sequences which are cloned from an immunized source and those cloned from a non-immunized source. This is not merely a process difference. Due to the immunization reaction, the libraries according to Ghahroudi will be enriched in antibodies that bind to the antigen that was used for immunization. The applicants' libraries are not enriched with one specific family of antibodies but contain the antibody variety that is present in the non-immunized source. This means that there is a high diversity within the claimed libraries. It is surprising that this diversity is obtained in the absence of light chains because this theoretically creates a lower diversity in the library. Clearly, in the circumstances, the applicants' libraries are novel over, and unobvious from, Ghahroudi et al.

The Examiner is requested to reconsider the double-patenting rejection based on claims 1-7 of U.S. Patent 6,399,763. The applicants consider that the respective sets of claims are patentably distinct. However, in order to simplify the issues and expedite allowance, a terminal disclaimer is being submitted herewith with respect to U.S. 6,399,763.

Favorable reconsideration of the application is requested in view of the foregoing.

Respectfully submitted,

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